

Gasoline sniffing and lead encephalopathy

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Gasoline sniffing is endemic in northern Manitoba and perhaps throughout much of northern Canada. Its most serious complication is lead encephalopathy, which can be fatal. Most of the toxic effects are thought to be due to tetraethyl lead and its metabolites. The specific treatment is chelation therapy, for which a protocol has been developed at the Health Sciences Centre, Winnipeg. Lead encephalopathy, however, is a manifestation of social, cultural and psychologic malaise.

L'inhalation d'essence est endémique dans le nord du Manitoba et, peut-être bien, à travers la plus grande partie du nord canadien. La complication la plus sérieuse est l'encéphalopathie au plomb, qui peut être fatale. On croit que la plupart des effets toxiques sont dus au tétraéthyle de plomb et à ses métabolites. Le traitement spécifique se fait par chélation, traitement pour lequel un protocole a été mis au point au Health Sciences Centre de Winnipeg. Toutefois, l'encéphalopathie au plomb représente une manifestation d'un malaise social, culturel et psychologique.

In 1941, when Machle¹ reviewed the physical findings, laboratory data, pathological features and prognosis of gasoline poisoning, no specific treatment was available. Scattered cases had been reported since 1895, but it was not until the 1950s that deliberate gasoline sniffing in adolescents was recognized as a problem.²⁻¹⁰ The treatment of lead encephalopathy began in that decade with the use of a chelating agent, ethylenediamine tetraacetic acid (EDTA). The case-fatality rate with EDTA alone had been 25%, but Chisolm¹¹ reported no deaths at all in 24 cases when it was used in combination with dimercaprol. These two agents along with d-penicillamine,¹¹ are currently in use at the Health Sciences Centre in Winnipeg.

It has been difficult to gather epidemiologic data on gasoline sniffing in Manitoba, and studies from elsewhere in the world are few.¹²⁻¹⁶ In 1975 Boeckx and associates¹⁷ found that in the isolated Indian community of Shamattawa, Man., there were 340 children between 4 and 18 years of age. Of these, 180 to 200 were either currently sniffing gasoline or had done so within the previous 3 months; the prevalence in this age group was thought to be nearly 100%. In a second native community in Manitoba, Little Grand Rapids, 50% of the children studied showed depressed levels of aminolevulinic acid dehydrase (ALAD), an enzyme inhibited by tetraethyl lead.¹⁷ Apparently the abuse of gasoline has

not declined in these or other northern communities since 1975. The problem is endemic.

Tetraethyl lead poisoning

Pathophysiologic and toxicologic aspects

The acutely poisoned gasoline sniffer manifests signs of encephalopathy — nervous irritability, anorexia, pallor, tremor, nausea, vomiting and delirium.¹⁷ The gasoline itself can cause acute pneumonitis, and death may ensue from a combination of central nervous system depression, respiratory irritation and bronchiolar obstruction.¹

The fuel contains four main groups of toxic compounds: paraffins, olefins, naphthenes and aromatic hydrocarbons, including benzene, toluene and xylenes. Benzene can cause bone marrow depression. Tetraethyl lead is added to gasoline as an antiknock compound, and such leaded fuel is used throughout the North, especially in snowmobiles and outboard motors. It is uncertain which neurologic and psychiatric signs and symptoms are caused by lead and which by hydrocarbons, but the half-life of hydrocarbons in the central nervous system is thought to be short.

It is also not known whether organic lead poisoning is caused primarily by tetraethyl lead, by its metabolites triethyl lead and inorganic lead, or by a combination of the three.¹⁸ Furthermore, the distribution of tetraethyl lead in the body is not fully understood, and it may differ from that of inorganic lead.

Diagnosis

The diagnosis can be made clinically when there is a history of gasoline sniffing. Severely affected patients are easily recognized even though there is no fixed constellation of signs and symptoms. Experience and the development of sensitive laboratory tests have simplified the differential diagnosis of lead poisoning (which includes choreiform disorders, rheumatic fever and encephalitis).

The typical neurologic situation in acute poisoning is one of cerebellar dysfunction, with mixed choreo-athetoid movements of the hands, arms, facial muscles and extensor tendons of the feet.

In a study of 50 patients who had been sniffing leaded gasoline Seshia and colleagues¹⁹ noted seven neurologic signs that were present in at least 20% of the group at the time of initial assessment (Table I). Of the 50 patients 4 had seizures; none had defects of sensation.

Lead encephalopathy has at times simulated both cerebral neoplasm²⁰ and a functional psychiatric disorder.^{9,21} In one of my cases a previously unreported complication, acute urinary retention, appeared. It would seem that almost any autonomic or peripheral neuropathy can occur transiently. Nonspecific findings

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may include bradycardia, transient neutrophilia, mild fever and irregular respiration.¹

The patient also shows psychiatric abnormality in the form of an organic brain syndrome that meets established criteria for delirium.²² Clouding of the sensorium is noted, with a marked deficit in attention and concentration. Although often difficult to assess, the patient has hallucinations and appears to be in a state of chaotic reverie. Speech is often incoherent. The symptoms and signs fluctuate from hour to hour, and the degree of psychiatric involvement is not correlated with the blood lead levels.

Tetraethyl lead depresses heme biosynthesis at two specific points in the pathway, thus providing biochemical markers useful in determining severity of poisoning and in providing an indication of the patient's response to chelation therapy. The activity of both ALAD and heme synthetase is reduced, although ALAD is the more sensitive indicator.^{17,23} In their study Boeckx and associates¹⁷ found that the mean ALAD activity in gasoline sniffers was one third the mean in the control group. Because ALAD activity is reduced before the blood lead level rises into the pathologic range, the enzyme can be used in screening for lead poisoning.¹⁷ It would also provide a baseline measurement in any prospective study.

The blocks in biosynthesis cause heme precursors to build up, and these too can be measured in blood and urine. The level of free erythrocyte protoporphyrin is increased in cases of lead encephalopathy and provides a second reliable indicator of the degree of poisoning.

The EDTA mobilization test can also be used: 500 mg/m² of EDTA, to a maximum of 1 g, is given intravenously in a solution of 5% dextrose in water over 1 hour. This is followed by assay of a 24-hour urine collection for lead: a ratio of the lead content (in micrograms) to the amount of EDTA administered (in milligrams) that is greater than 1 is considered positive.

Management

In Manitoba, patients who need chelation therapy are evacuated from remote areas to the Health Sciences Centre in Winnipeg. This is done if the blood lead level exceeds 1.95 $\mu\text{mol/l}$ or if encephalopathy is detected. The exact form of treatment is determined by the blood lead level, the presence or absence of encephalopathy and the results of an EDTA mobilization test (Table II). The electroencephalogram and electrocardiogram do not provide diagnostic information. Chlordiazepoxide and phenobarbital are generally used for sedation.

Social context of gasoline sniffing

It is generally agreed that the medical aspects of gasoline sniffing and lead encephalopathy are acute manifestations of more basic social, psychologic and cultural malaise. Sociologic studies of gasoline sniffing have shown that the children who abuse gasoline do indeed come from poor, socially disorganized families; they have few facilities for recreation and they may sniff gasoline because of peer pressure and a lack of positive role models.²⁴ Nurcombe and coworkers¹⁶ suggest that this kind of impoverished home and community life

causes what they call a hunger for stimuli. They feel that among their subjects, the Australian aborigines of Arnhem Land, many may use gasoline as a release from the anxiety caused by culture-specific stresses. In northern Canada too, the drive toward gasoline sniffing must be understood in a historical and cultural context, since most of the children involved are natives.

Barnes^{25,26} found that one of the most significant correlates of gasoline sniffing was parental alcohol abuse. For the children gasoline is simply the cheapest and handiest intoxicant on the reserve. We must note, however, that even in some northern communities where substance abuse is considerable, gasoline sniffing is virtually unknown. In a survey of 5 years of outpatient files at five locations in the Northwest Territories, for instance, I did not encounter a single confirmed case of gasoline sniffing, yet alcohol was widely overconsumed in those same communities.²⁷ Similarly, in a study of Pueblo schoolchildren Kaufman¹² found that the gasoline sniffers and control children belonged to equally disturbed families. None of the obvious factors, then, can account for the phenomenon; they are really only correlates.

Currently, therapeutic intervention by physicians in Manitoba is not entirely successful. Many patients repeatedly enter hospital with lead encephalopathy, and no one knows whether chelation therapy has significantly improved their neuropsychologic status beyond the short term. Since such treatment can be dangerous, this is an important issue. The chelating agents themselves may be teratogenic. Since many of the patients are sexually active, all postmenarchal women are screened with a pregnancy test.

Delicate social and political issues are raised by gasoline sniffing. For instance, what are the moral and legal rights of a fetus whose mother is sniffing gasoline?⁶ Hunter and collaborators²⁸ believe, on the basis of their study of Shamattawa infants, that there may be a fetal gasoline syndrome, characterized by profound

Table I—Neurologic signs in 50 patients with lead encephalopathy¹⁹

Sign	No. of patients
Abnormally brisk deep-tendon reflexes	34
Intention tremor	29
Postural tremor	28
Abnormally brisk jaw jerk	28
Abnormal heel-to-toe test	13
Ataxia when standing on one foot	11
Ataxia when standing on two feet	10

Table II—Criteria for treatment of lead poisoning

Serum lead level ($\mu\text{mol/l}$)	Encephalopathy	Result of EDTA mobilization test	Treatment
0–1.95	–	–	–
1.95–3.80	–	–	–
1.95–3.80	–	+	d-penicillamine or EDTA and penicillamine
Any level	+	+ or –	dimercaprol, EDTA and penicillamine
> 3.80	+ or –	+ or –	dimercaprol, EDTA and penicillamine

retardation, initial hypotonia progressing to hypertonia, scaphocephaly, a prominent occiput, poor postnatal growth and other lesser anomalies. Such a syndrome would be the most frightening consequence of gasoline sniffing; in some communities an entire generation may be inflicting irreversible damage on itself and its offspring.

Hunter and collaborators also observed that Shamattawa was built in 1949 and that a few years later the band split, half of it forming the community of York Landing. In York Landing "there has not been a gasoline abuse problem of note,"²⁸ and no cases of fetal gasoline syndrome were suspected. These two communities may provide study and control groups for worthwhile investigations.

Conclusions

Many patients with this form of lead poisoning are known gasoline sniffers, and they may even smell of gasoline upon presentation. Since the habit can be acquired at a very early age, lead poisoning should be suspected in the North whenever a patient more than 5 years old shows neurologic or psychiatric signs and symptoms. The physician must be prepared for atypical presentations.

The patient's problems, however, are not purely medical, so chelation therapy must be only one facet of an overall approach. Although lead encephalopathy resembles the acute complications of alcoholism, the damage is more severe and more quickly done, and the patients are often children. Comprehensive study and effective management are urgently required.

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